molecules, the enzymes they encode, and transformed plants including said nucleic acid molecules would clearly be most efficiently searched together. As Section 803 of the MPEP directs, "[i]f the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions." Moreover, a serious burden would arise if the application remains restricted. For the foregoing reasons, Applicants maintain their traversal of the restriction requirement.

II. Specification

The title of the invention has been objected to as allegedly not being descriptive of the claimed invention. As the claims are now directed to nucleic acid molecules encoding an enzyme in the methionine degradation pathway, the title has been so amended. As such, withdrawal of this objection is respectfully requested.

III. Rejection under 35 USC § 101, Utility

Claims 1-2 and 12-13 stand rejected under 35 USC § 101 for allegedly not being supported by either specific and/or substantial utility, or a well-established utility. This rejection is respectfully traversed for the reasons which follow.

In support of this rejection, the Office Action asserts:

> [t]he claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of these compositions are not specific and are generally applicable to any nucleic acid. . . Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compounds(s) such that another non-asserted utility would be well established for the compounds.

Office Action mailed October 2, 2001, Paper No. 13, pages 3-5.

It is well-established that "when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983). The present specification describes many

objectives that are met by the present invention including, but not limited to providing a substantially purified nucleic acid sequence which encodes a maize or soybean enzyme or fragment thereof, wherein the enzyme is a methionine adenosyltransferase (e.g., SEQ ID NO: 1). *See Specification*, Summary of the Invention, page 22.

The Office Action further asserts that:

> It is noted that applicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence.

Office Action mailed October 2, 2001 at page 5.

The specification provides extensive evidence based on sequence identity (Table A) that the disclosed genes encode polypeptides having specified enzymatic activity. The specification also indicates by way of EC Classification designation that the specified enzyme is of an enzymatic classification well-known in the art. Further, a detailed description of the characterization of the specified enzyme, as well as the identification of such enzyme from other plant sources is provided in the specification. *See, e.g., Specification* at page 10-11. As such, it is submitted that the functionality of the claimed nucleic acid molecules is disclosed. Further, based on the background provided regarding the functionality and structural characteristics of the claimed enzyme, it is submitted that sequence homology is indeed an adequate and predictable indicator of such functionality. Thus, based on such teachings, one of ordinary skill in the art would immediately appreciate the usefulness of the claimed nucleic acid molecules.

An examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Federal Register 66(4):1096, Utility Guidelines (2001).

"[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996).

As such, an examiner "must do more than question operability – [the examiner] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 USPQ 664, 666 (CCPA 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); MPEP § 706.03(a)(1). No such factual reasons have been provided. The utilities disclosed by Applicants must be accepted as factually sound unless and until the Patent Office provides factual reasons that undermine the credibility of the assertion. Therefore, the Office has not met the requisite burden to impose a 35 USC § 101 rejection.

The Office Action alleges that "several publications document the unpredictability of the relationship between sequence, structure, and function." *Office Action mailed October 2, 2001* at page 6. However, none of the references cited in the Office Action specifically relate to the claimed enzyme or the methionine pathway in general. Further, Applicants refer the Office to the following articles where it is equally well-established that sequence similarity is routinely used by those of ordinary skill in the art as a predictor of function. *See, e.g.,* Venter, *et al.*, The Sequence of the Human Genome, Science, 291: 1304-1351 (2001); Woese, *et al.*, Conservation of Primary Structure in 16S rRNA, Nature, 254: 83-85 (1975).

In sum, Applicants have asserted substantial, specific utilities for the claimed nucleic acid molecules of the invention, and absent specific evidence to the contrary, this assertion must be accepted. Additionally, Applicants have asserted a number of utilities for which the nucleic acids molecules of the invention can be used. These include, but are not limited to, determining the expression levels of the methionine adenosyltransferase (pages 36-39); detecting mutations in the genes encoding these enzymes (page 39-42); and producing plants with altered expression of these enzymes (page 42-47). As such, Applicants have met their burden in establishing specific, "real-world" utilities for the claimed invention.

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by specific and well-established utilities as disclosed in the specification. As such, withdrawal of this rejection is respectfully requested.

IV. Rejection under 35 USC § 112, 1st Paragraph, Enablement

Claims 1-2 and 12-13 stand rejected under 35 USC § 112, 1st Paragraph because the claimed invention is allegedly not supported by either a specific and substantial asserted utility or a well established utility, and thus one of ordinary skill in the art would not know how to use the invention. This rejection is traversed for the reasons discussed above with regard to the 35 USC §101 rejection. As such, it is submitted that the specification enables one of skill in the art to use the invention in accordance with the asserted specific and substantial utilities discussed above. Accordingly, withdrawal of this rejection is respectfully requested.

Moreover, it is submitted that the Examiner has not met the evidentiary burden to impose an enablement rejection for failure to enable one of skill to use the invention. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (*quoting In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA. 1971) (emphasis in original)). It is also well-established that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998) (emphasis added) (*quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991)).

The present specification indeed discloses how to use the claimed invention as discussed above. The Office Action has failed to provide specific evidence supporting this rejection, or any specific explanation of why the specification allegedly fails to enable these uses. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 USPQ 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

Accordingly, for at least these reasons, the enablement rejection under 35 USC § 112, 1st paragraph, is traversed, and withdrawal of this rejection is respectfully requested.

V. Rejection under 35 USC § 112, 1st Paragraph, Written Description

Claims 1-2 and 12-13 also stand rejected under 35 USC §112, 1st paragraph, as allegedly containing subject matter which was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time of filing. This rejection is respectfully traversed for at least the following reasons.

The Office Action acknowledges that SEQ ID NO: 1 meets the written description requirement. However, in support of this rejection, the Office Action alleges:

> claims 1-2 and 12-13 are directed to encompass gene sequences, and fragments of sequences of SEQ ID NO: 1, corresponding sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth.

Office Action mailed October 2, 2001 at page 7.

Initially, the purpose of the written description requirement is simply to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *See Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 USPQ2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, v865 F.2d 1247, 1251, 9 USPQ2d 1461, 1464 (Fed. Cir. 1989).

A related and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 USPQ 323, 326 (CCPA. 1981)). Thus, simply because the claimed nucleic acid sequences may also include sequences from other species does not require that Applicants describe each and every one of these molecules. Further, "a description as filed is presumed to be adequate, unless and until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption." *Federal Register* 66(4):1107, Written

Description Guidelines (2001). In this regard, the Examiner is required to disclose "express findings of fact which support the lack of written description conclusion." *Id.*

The present claims are directed to the genus of nucleic acid molecules which encode a specified *maize or soybean* enzyme, or fragments of such enzyme. Applicants have provided detailed chemical structures of the claimed nucleic acid sequences, as well as additional information about the encoded enzymes. These sequences provide "structural feature[s] possessed by members of the [claimed] genus that distinguish them from others." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). In contrast to the mere name "cDNA" provided in *Eli Lilly*, Applicants have provided detailed chemical structures. For at least this reason, it is respectfully submitted that the present claims meet the written description provision under 35 USC § 112, 1st paragraph.

The use of open claiming language (comprising) or semi-open claiming (consisting essentially of) does not alter the fact that a skilled artisan would readily envision adequate written description support. The fact that nucleic acid sequences may be added to either end of the recited sequence is beside the point. Applicants have therefore reasonably conveyed to one skilled in the art possession of the claimed invention, even when additional sequences are added to either end. Indeed, as disclosed in the specification on pages 53, the addition of, for example, detectable labels or extra nucleotides is readily envisioned by those of ordinary skill upon reading the present specification.

Additionally, "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'" *Eli Lilly* at 1569. In the present case, it is submitted that the disclosure of an extensive number of nucleic acid sequences encoding the specified enzyme or fragments thereof, *e.g.,* SEQ ID NOS: 1-429 and 1635-2479, in combination with "other appropriate language" in fact does provide sufficient written description for claims within the genus. Such "other appropriate language" is found, *e.g.*, in the form of sequence identity and numerous methodologies to obtain additional sequences. Therefore, it is clear that one of ordinary skill in the art would recognize that Applicants were in possession of the genus of the specified *maize and soybean* enzyme encoding genes.

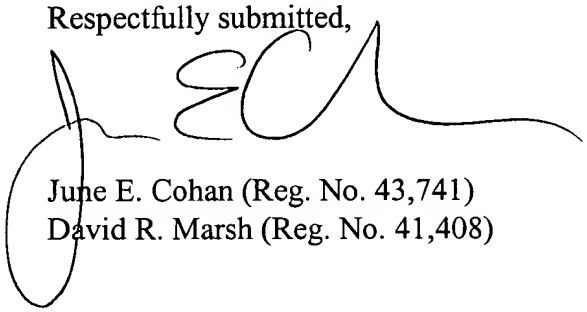
Accordingly, for at least the foregoing reasons, the rejection under 35 USC. §112, 1st paragraph, written description, is traversed, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance, and notice of such is respectfully requested.

The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



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Marked up version of the specification and claims

In the title:

Please cancel the title and replace it with the following:

Nucleic Acid Molecules [and Other Molecules] Associated with the Methionine [Synthesis and] Degradation Pathway[s]

In the specification:

On page 17 of the specification, please delete the second paragraph beginning with "Similarity analysis includes," and replace it with the following amended paragraph:

Similarity analysis includes database search and alignment. Examples of public databases include the DNA Database of Japan (DDBJ) [(http://www.ddbj.nig.ac.jp/);] (www.ddbj.nig.ac.jp); Genebank [(http://www.ncbi.nlm.nih.gov/Web/Search/Index.htlm);] (www.ncbi.nlm.nih.gov/Web/Search/Index.html); and the European Molecular Biology Laboratory Nucleic Acid Sequence Database (EMBL) [(http://www.ebi.ac.uk/ebi_docs/embl_db/embl-db.html)] (www.ebi.ac.uk/ebi_docs/embl_db/embl-db.html). Other appropriate databases include dbEST [(http://www.ncbi.nlm.nih.gov/dbEST/index.html)] (www.ncbi.nlm.nih.gov/dbEST/index.html), SwisProt [(http://www.ebi.ac.uk/ebi_docs/swisprot_db/swisshome.html)] (www.ebi.ac.uk/ebi_docs/swisprot_db/swisshome.html), PIR [(http://www-nbrt.georgetown.edu/pir/)] (www.nbrt.georgetown.edu/pir), and The Institute for Genome Research [(http://www.tigr.org/tdb/tdb.html)] (www.tigr.org/tdb/tdb.html).

In the claims:

1. (Amended) A substantially purified nucleic acid molecule that encodes a maize or a soybean enzyme or fragment [thereof] of said maize or soybean enzyme, wherein said maize or soybean enzyme is [selected from the group consisting of:

(a)] methionine adenosyltransferase[,

(b) S-adenosyl-methionine decarboxylase,

(c) aspartate kinase,

(d) aspartate-semialdehyde dehydrogenase,

(e) cystathionine gamma-synthase,

(f) cystathionine beta-lysase, and

(g) 5-methyltetrahydropteroyltriglutamate-homocysteine-S-methyltransferase].

2. (Amended) The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises [a] the nucleic acid sequence [selected from the group consisting] of SEQ ID NO: 1 [through SEQ ID NO: 3204].